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Interaction effects of different drivers of wild bee decline and their influence on host–pathogen dynamics

Ivan Meeus, Matti Pisman, Guy Smagghe and Niels Piot

Wild bee decline is a multi-factorial problem, yet it is crucial to understand the impact of a single driver. Hereto the interaction effects of wild bee decline with multiple natural and anthropogenic stressors need to be clear. This is also true for the driver 'pathogens', as stressor induced disturbances of natural host–pathogen dynamics can unbalance settled virulence equilibria. Invasive species, bee domestication, habitat loss, climate changes and insecticides are recognized drivers of wild bee decline, but all influence host–pathogen dynamics as well. Many wild bee pathogens have multiple hosts, which relaxes the host-density limitation of virulence evolution. In conclusion, disturbances of bee-pathogen dynamics can be compared to a game of Russian roulette.

Address
Department of Crop Protection, Ghent University, Ghent, Belgium

Corresponding author: Meeus, Ivan (ivan.meeus@UGent.be)

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Introduction

The treasure chest of life, Earth's biodiversity, is under pressure. Population declines and extirpations are of the magnitude to call it the sixth major extinction event [1]. This biological annihilation impairs ecosystem services. Insect pollination underpins plant-derived ecosystem services supporting the seed set in 85% of all flowering plants [2], but direct human benefits are also gained with pollination of 76% of the leading agricultural crops [3]. Insect pollination is performed by different families of insects; herein bees (the Apiformes within the superfamily Apoidea) are the most exemplary as the nutritional needs of all their life stages are fully dependent on nectar and pollen [4].

The decline of insect pollinators, especially wild bees, is acknowledged worldwide [5,6]. A full overview of the population decline of wild bees, their status and of the drivers thereof fall outside the scope of this review. For this we refer to the report by the International Platform on Biodiversity and Ecosystem Services and the references therein [7,8].

Wild bee decline is often described as a multi-factorial problem. While this is true, it is also an evasive answer. In order to further comprehend this complex puzzle, three things are essential: firstly, it is important to understand the impact of single drivers within an environmental context where multiple natural and anthropogenic stressors act on wild bee populations [9]; secondly, these drivers are expected to show interaction effects which can be antagonistic or synergistic [10]; thirdly, the impact of drivers can differ based on the target species. For bumble bees the interaction among pathogens, pesticides, and diet is identified as the most crucial stressor. Although bumble bees are the best monitored wild bee species, we still only have patchy and incomplete evidence of the specific role of different drivers of bumble bee decline, with challenges associated with the setup of environmentally realistic experiments to study interacting stressors [11].

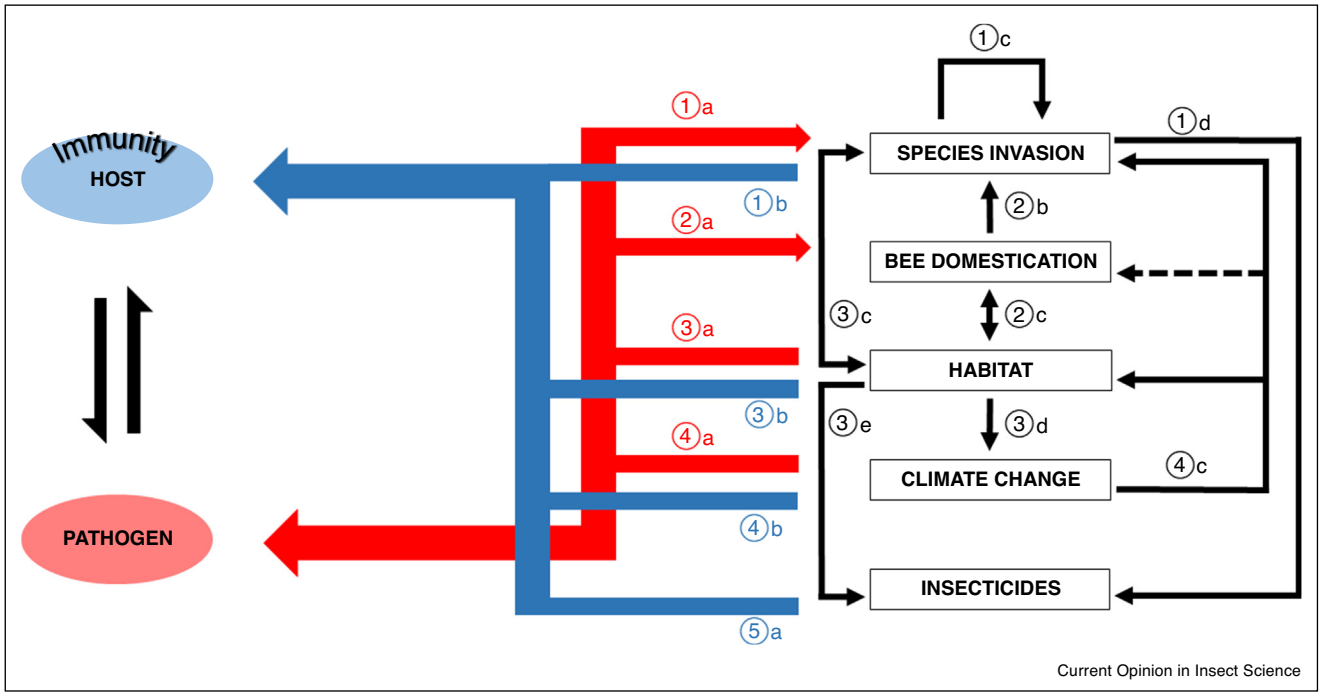
Here we will address the interaction effects of drivers of wild bee decline with the stressor parasites and viruses (from here on referred to as pathogens). When talking about bee pathogens one must recognize the historical context and knowledge gathered from the domesticated western honey bee, *Apis mellifera*. For example, the term honey bee viruses is persistently used, while most of these viruses have a much larger host-range and for many of them the honey bee will most likely not even be the prime host [12]. Another consequence of honey bee diseases as a key information source is a biased view on host–pathogen dynamics. In domesticated animals a pathogen is sometimes considered as an aberrant factor, which needs to be eradicated. In a natural ecosystem, however, pathogens play an important role [13]. In an undisturbed natural ecosystem the population size of a species fluctuates around the environment's carrying capacity. The population size is driven by bottom-up forces such as food and nesting availability. Top-down forces such as predation and pathogens negatively affect the population size. The driver of wild bee decline called 'pathogens or parasites' should therefore be seen in the context of factors which disturb natural host–pathogen dynamics. Pathogens are often not the main player regulating the population size [14] and have often evolved a

virulence equilibrium with their hosts [15]. However, disturbance of the natural ecosystem can unbalance this virulence equilibrium, increasing the role of pathogens as a top-down force on a population. In extreme cases pathogens can cause dramatic declines in host populations and eventually lead to host extinction [16].

The influence of drivers of wild bee decline on host–pathogen dynamics

In Figure 1 we give an overview of some widely reported drivers of wild bee decline. These drivers have a direct influence on wild bee populations, but also have the potential to cause interaction effects. Interactions can be synergistic, but shared occurrence of drivers can also be neutral or antagonistic [10]. It is important to make a distinction between two types of interaction effects: firstly, interaction modification effects and secondly, interaction chain effects. Interaction modification effects can be defined as the effect of one driver which decreases (antagonistic) or increases (synergistic) the impact of a second driver. Interaction chain effects are defined as a direct linkage between two drivers, where one driver

Figure 1



Overview of the drivers of wild bee decline. Coloured arrows represent a direct interference of drivers of wild bee decline with natural host–pathogen dynamics (and are explained in the main text). The black arrows represent interaction chain effects. There is a long history of honey bee domestication. Different genetically distinct lineages of *Apis mellifera* from Africa, Asia and Europe have been introduced into other regions. The introduction in North America dates back to 1622; with later introductions in South America around 1956 [55]. Also intentional introduction of bumble bee species occurred in for example New Zealand and Chile [56]. Currently different bumble bee species are reared for commercial pollination purposes, and in the early 1990s also *Bombus terrestris* introductions in non-endemic regions were reported [20] (arrow 2b). The hives of honey bees placed at mass flowering crop (MFC) for pollination services also visit adjacent natural habitats. Especially after MFC bloom plant–pollinator networks and seed set in natural habitats is influenced [57,58]. This effect can be seen as a direct impact on host–pathogen dynamics by influencing transmission dynamics at flowers, or indirect impact by influencing the habitat. Domesticated honey bees will also have an effect on the seed set of plant species (arrow 2c). The loss of wild bee diversity and abundance caused by habitat loss, increases the pollination gap [59]. We speculate that this pollination gap is often compensated for with the use of more domesticated pollinators, such as honey bees (bidirectional arrow 2c). Loss of habitat has the intrinsic potential to have interactive chain effects with all drivers of wild bee decline. The invasion success of a species is linked to landscape composition [18]. The existence of invader complexes, where both invading plant and pollinator interact, leads to mutual positive feedback, further underline arrow 3c. Morales and Aizen (2006) reported such complexes, with a significantly closer association of invasive flower visitors with invasive plants than with native plants [60] (arrow 1c). Habitat changes such as deforestation, urbanization and agricultural intensification clearly have an effect on the progression and magnitude of climate change (arrow 3d) [61,62]. Arrow 3e entails the exposure to insecticides in flowering crops which is higher when fewer (semi-)natural foraging opportunities are present. Negative effects on wild solitary bees weakened as percentage of semi-natural habitat increased; here both interaction modification effects and interaction chain effects can play [63•]. Climate change has interaction chain effects on the other drivers of wild bee decline (arrow 4c). It has been reported that climate change will influence plant (influence on habitat) and pollinator communities (influence on invasive species) (as reviewed by [39]). The effect of climate change on the use of domesticated species for pollination, that is, further loss of natural pollination services and increased use of domesticated species, remains unexplored to our knowledge. Insecticides are used worldwide to eradicate or constrain pest populations. Often invasive species form a major threat to agricultural income and pesticides are one of the most common measures to eradicate or control them [64] (arrow 1d).

influences the abundance, but not the per capita/unit impact, of a second driver [17]. One example of interaction chain effects is an increased abundance of invasive species facilitated by habitat modification [18]. Here, the per capita impact of an invasive individual remains constant, but the increased abundance results in a larger impact overall.

In this review we focus on how these drivers can disrupt existing natural host–pathogen dynamics, as this is most threatening for the local existence of a population. The interaction of the drivers with the specific stressor 'pathogens' is depicted in Figure 1. In order to understand the potential mechanism behind a certain interaction we made a distinction between, firstly, direct interference (coloured arrows) and secondly, interaction chain effects (black arrows). Within the direct effects we made a distinction between effects that either impact the host or the pathogen. Drivers that directly impact the host mostly impair the immunity of the host (blue arrows). Direct effects on the pathogens (red arrows) include the impact on the pathogen's life cycle, infectivity, transmission ability, etc. Interaction chain effects are mainly explained in the figure legend. Interaction modification effects are not visualized in Figure 1, as general empirical evidence is very scarce. Nonetheless we do not regard these effects as unimportant.

Species invasion

Species invasion and its relationship to pathogens has been mainly studied in the context to explain invasion success. A well-studied example of disease-mediated invasion (DMI) (arrow 1a) is the replacement of red squirrels in the UK by grey squirrels from North America. Here, the squirrel pox virus causes high mortality in native red squirrels [19]. Such allopatric introductions of pathogens to previously unexposed hosts are considered as a main threat to wild bees as well [20]. While many pathogens of invasive species will not find new suitable hosts [21], those that do have a higher likelihood to infect species with a close phylogenetic relationship to the original host [19].

Invasive species can thus act as a reservoir for pathogens which spill-over to native species, with close phylogenetically related species being most at risk. Secondly, spill-back dynamics, where invasive species act as a new host for native pathogens, should also be considered [22]. However, an invasive species can also be a less suitable host for native pathogens. In this case, no increased spread of pathogens will occur and a dilution effect can take place, with the invasive species acting as a pathogen sink or dead-end host [23]. Finally, native pathogens may also impact the fitness of invasive species, as described by the biotic resistance hypothesis (arrow 1a opposite direction) [24••]. However, this hypothesis still remains to be proven.

Aside from invasive bee species, invasive plant species can also directly influence native pollinators [25]. Influence on nutrition and health status can have a direct impact on the host (arrow 1b); while host–pathogen transmission can be influenced indirectly through changes in insect-flower interactions, as well as changes at the wild bee population and community level (arrow 1a).

Bee domestication

Domestication of endemic bee species (e.g. honey bees and bumble bees) can have a direct impact on pathogens in wild bee populations (arrow 2a). Like invasive species, domesticated species can potentially act as a reservoir for specific pathogens, potentially driving disease-induced extinction [26]. Immune competence of domesticated species should also be considered, as impaired immunity could drive spill-back dynamics. Disturbance of wild bee pathogen dynamic equilibria by domesticated species has been observed in several studies [27–29]. Yet the underlying mechanism driving this disturbance remains undetermined. When looking from the other perspective, wild bees can also act as a reservoir for domesticated species (arrow 2a).

Habitat loss

Habitat changes can affect both pathogens and hosts at different spatial scales. At the larger scale, landscape changes can affect pathogen spread [30]. Habitat changes can affect both the movement patterns and density of hosts and will in turn also affect higher trophic levels, like pathogens and pathogens, which are even more susceptible to habitat changes [31,32].

At the local scale, habitat loss, which includes loss of floral resources and suitable nesting sites, has a dual effect. First, it can affect the pathogens and their transmission (arrow 3a). Flowers are seen an important location for transmission of pathogens between bee species [33,34]. Reduction in floral resources changes plant–pollinator networks, forcing pollinators to forage on a lower amount of flowers. This increases the visitation frequency and the inter-species and intra-species contact on the flowers, which in turn increases the potential of transmission via flowers. Reduction in floral resources can also decrease the local wild bee diversity. These alterations in host presence and abundance can again affect pathogen transmission and dynamics, in similar ways as described above for the landscape scale. Secondly, habitat changes can directly affect the host. Reduction or loss of floral resources decreases the amount of available (qualitative) nutrition which can have an effect on bee immunity and fitness in general [35,36] (arrow 3b). This in turn can increase the host's vulnerability to pathogen infections [37•]

Climate change

The biological effects of climate change are recognized as a threat for biodiversity [38]. Climate change can institute plant pollinator mismatches, as plant and pollinator phenology can be driven by different environmental cues or thresholds [39]. In general it is believed that generalist species will be less affected and may even profit from climate change.

It is clear that host–pathogen dynamics can be influenced by changing climate conditions (e.g. temperature, precipitation and seasonality). Different weather conditions can influence the transmission and infection success of pathogens (arrow 4a) [40•]. Temperature is also an important factor affecting the ability of pathogens to complete their life cycle. In the case of *Nosema ceranae*, which infects both *Apis* and *Bombus* species, viability of spores is rapidly lost when exposed to freezing temperatures [41]. The reduced *N. ceranae* spore germination at low temperatures could be important to explain the different epidemiology and impact of *N. ceranae* and *Nosema apis* on honey bees, where the latter is more adapted to a cold environment [42]. The life cycle within the honey bee host is also influenced by temperature, where *N. ceranae* is better adapted than *N. apis* to complete its life cycle in honey bees at different temperatures [43]. Similar effects can be expected in wild bees and their parasites.

The most clear effect of changing weather conditions is the impact on foraging ability, with impaired nutritional status reducing the bee's tolerance to pathogens (arrow 4b) [35,36,37•].

Insecticides

It is often difficult to translate lab data or reported sub-lethal effects into hard evidence of impacts on wild bee communities. The debate on the effects of neonicotinoids is a clear example here [44,45]. The use of realistic field concentrations (i.e. concentrations in the nectar and pollen), realistic timing as well as exposure time are important aspects to understand pesticide impacts. Field realistic experiments are crucial, yet it remains important to realize that sub-lethal effects can still remain undetected [46••]. Also effects in model species are not always transferable to other bee species [47], and country-specific effects of neonicotinoids on honey bees and bumble bees suggest that interacting factors are involved [48]. We here focus on the off-target effects of insecticides (and other pesticides) on host–pathogen dynamics (arrow 5a). Although the effects of neonicotinoids on wild bees is reported [47,48] and multi-species dynamic Bayesian occupancy analysis found negative effects on wild bee persistence in relation to exposure to neonicotinoids of oilseed crops [49], no data on the relation with pathogens has been reported. Below data are restricted to the honey bee. It has been shown that the neonicotinoid clothianidin can impair NF-κB signalling and increase viral titres in honey bees [50]. Fipronil (phenylpyrazole) and thiacloprid influence honey bee mortality caused by *Nosema cerenae* [51]. We do not argue that both herbicides and fungicide are harmless, yet we restrict ourselves to the insecticides as these most likely have the most severe direct effect.

Another layer of complexity

In disease models with single host pathogens and density-dependent transmissions the pathogen goes extinct before the host. However, disease induced mortality does exist; stochastic events in small populations, deviations from the density-dependent transmission assumption are proposed mechanisms [26]. A multi-host–pathogen can escape the host density limitation and can drive less adapted hosts to extinction; for example high density of host A supports higher pathogen densities, increasing the detrimental effects on host B [52]. Although the principle of pathogen mediated competition is logical and simple, empirical data is often lacking and difficult to gather. An interesting question is if the differences in life style between solitary and social pollinators could trigger differences in relative timing of transmission and mortality onset, as both are important in the evolution of pathogen virulence [53].

In natural conditions a wild bee can be infected with multiple pathogens. Pathogens can influence the infection success, transmission and virulence of each other [54]. Where each pathogen by itself may be influenced by different drivers to a different extent. The presence of multiple pathogens within a host and their interactions increase the difficulty of assessing the effects of different drivers on pathogen host dynamics. Moreover it is often hard or even impossible to extrapolate results of local studies as both the pathosphere, the host assembly and local effects of other drivers are location specific.

Conflicts of interest statement

None.

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Park *et al.* investigated the interaction effect between semi-natural habitat and intensity of pesticide usage on biodiversity and abundance of wild pollinators in apple orchards. They found a negative effect of pesticide usage on solitary bees, but not social wild bees. However, this negative effect weakened as percentage of semi-natural habitat increased. Whether this buffer effect was caused by an increased abundance in resources or by semi-natural elements providing refuge was not determined. However, this study indicates a second, indirect positive effect of semi-natural habitats for solitary bees and the importance of incorporating interaction effects between pesticides and other drivers of bee decline.

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